

The effect of supraclavicular brachial plexus blockade on Bispectral index (BIS): a pilot study

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Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof, that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

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Abstract

Background: Many studies have demonstrated that neuraxial (spinal and epidural) anesthesia decreases level of consciousness.¹⁻³ Plausible causal theories relate to afferent spinothalamic tracts suppression, rostral neuraxial spread of local anaesthetics, and systemic local anaesthetic effects.¹⁻³ No study has thus far interrogated the effect of non-neuraxial loco-regional anesthesia on level of consciousness.

Methods: Un-premedicated ASA 1 patients undergoing elective hand surgery (n=20) were administered ultrasound-guided supraclavicular brachial plexus blocks using 2mg/kg of 0.5% bupivacaine. A pre-block numeric pain visual analogue score was performed. No sedation was administered. Bispectral index (BIS) control readings were obtained before brachial block. For an hour after the block, the lowest BIS readings, within each subsequent 10minute interval was documented. Over the 60minute observation period, a decrease in BIS reading was considered as being any change of $BIS \leq 80$.

Results: In the hour post-block, BIS values ≤ 80 occurred in 65% (CI^{95%} 40.4 to 83.6%) of patients when compared to their pre-block (control) BIS values. This result did not correlate to age, gender or the nature of the illness requiring surgery (traumatic versus pre-existing, chronic illness). There was no difference in the mean pre-block pain scores between the patients who experienced a drop in $BIS \leq 80$ and $BIS > 80$ with mean values of 2.45 (IQR; CI^{95%}) and 2.44 (IQR; CI^{95%}) respectively (two-sample Wilcoxon rank-sum test, $p = 0.9022$).

Conclusion: Brachial plexus blockade itself, in the absence of sedative drugs, reduced BIS. This is consistent with light to moderate sedation.

Oorsig:

Agtergrond: Verskeie studies het gepostuleer en bewys dat neuraksiale (spinaal en epidurale) narkose die sentrale bewussynsvlak verlaag.¹⁻³ Die mees waarskynlike verklaring vir hierdie verskynsel is die onderdrukking van die afferente spinotalamiese neurlogiese bane, hoewel die rostrale verspreiding so wel as die sistemiese effekte van die lokale verdowingsmiddel, ook 'n beduidende rol mag speel.¹⁻³

'n Oorsig van die literatuur het geen spesifieke studies opgelewer wat die moontlike verwantskap tussen non-neuraksiale regionale narkose tegnieke en sentrale bewussynsonderdrukking evalueer nie.

Metodiek: Twintig (N=20) ASA 1 pasiente wat presenter het vir elektiewe handchirurgie, het non-neuraksiale regionale narkose in die vorm van 'n ultraklank begeleide supraklavikulere brachiaalpleksus senuweeblok ontvang. Geen premedikasie of enige ander vorm van orale of parenterale analgesie of sedasie is voor of tydens die prosedure toegedien nie. Die pasiente se sentrale bewussynsvlak is moniteer deur gebruik te maak van die BIS (Bispectral Index) monitering sisteem. 'n Basislyn lesing vir elke pasient is noteer voor die aanvang van die regionale senuweeblok, en die laagste BIS waarde vir opeenvolgende 10 minuut intervale tot en met 'n total van 60 minute is gedokumenteer.

Resultate: In 65% van ons steekproef van 20 pasiente is BIS waardes noteer wat beduidend is van 'n geringe tot matige vlak van sentrale bewussyn onderdrukking (BIS <80) (CI⁹⁵ = 40.4-83.6%). Geen korrelasie tussen ouderdom, geslag of die aard van die presenterende siektetoestand (akuut versus chronies) is demonstreer nie.

Slotsom: Ons studie het getoon dat non-neuraksiale regionale narkose (in die afwesigheid van enige ander vorm van analgesie of sedasie), 'n gering tot matige onderdrukking van die sentrale bewussyn kan induseer. Alhoewel hierdie loodsstudie nie aangedrewe was om 'n statisties betekenisvolle gevolgtrekking te lewer nie, beklemtoon dit wel die behoefte en potensiaal vir toekomstige studies om hierdie interessante verwantskap verder te ondersoek en te evalueer.

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1. Background

Many studies have considered and proven that neuraxial (spinal and epidural) anesthesia decreases the level of consciousness.¹⁻³ The most likely causal theory proposed is related to the suppression of the afferent spinothalamic tracts, although rostral spread, and systemic effects, of local anesthetic agents still feature as plausible causes.

No study appears to have specifically looked at the effect of non-neuraxial loco-regional anesthesia on level of consciousness.

2. Literature review

2.1. Benefits of loco- regional techniques in anesthetic practice

The beneficial impact of loco-regional anesthesia is widespread. For anesthetists, the advantages around cardio-respiratory stability, rapid postoperative recovery and the preservation of protective airway reflexes make regional anesthesia a very favourable tool of practice.⁴ Loco-regional anesthesia usually offers great post-operative analgesia, and avoids the sedative and other unwanted side effects of systemic analgesics. This is especially beneficial in patients with pre-existing medical conditions, where these side effects can be detrimental and delay recovery.⁵

Economic benefits to loco-regional anesthesia include reduced hospital length of stay, and a consequential reduction in the incidence of hospital acquired infections.⁶ Loco-regional techniques may beneficially reduce operative theatre pollution by reducing the amount of volatile general anesthetic used.⁵

The three main reasons cited by patients, for their preference of regional anesthesia over general anesthesia, were that they were awake during the procedure, that they could have family contact early post-operatively and that they take in food earlier.⁴ These benefits are impacted by patient's fear of pain from the needle puncture site while the procedure is being performed, fear of needles in general, and fear of recall of the entire surgical procedure.⁴

The question of co-administered sedation comes to light, and the validation of its use remains operator dependant.⁴

2.2. An overview of brachial plexus blocks: anatomy, approaches and techniques

The brachial plexus is formed by the anterior rami of the nerve roots from the fifth cervical to the first thoracic nerve root (C5-T1).⁷ (Figure 1)

Brachial plexus blocks are the most common major peripheral nerve blocks performed.⁸ Various approaches to brachial plexus blocks are available, including the interscalene, infraclavicular, supraclavicular and the axillary approach.⁸ Supraclavicular brachial plexus blocks (SBPB) are excellent for all types of upper limb surgery, including tourniquet placement.⁷ Due to its associated risk of haemothorax and pneumothorax, it has always been practiced with extreme caution. Since 1978, when the first attempt at a Doppler guided study was performed, the advancement with real time ultrasound-assisted blocks has increased the safety and quality of supraclavicular blocks. Consequently, many more blocks are being performed with good success rates.⁷

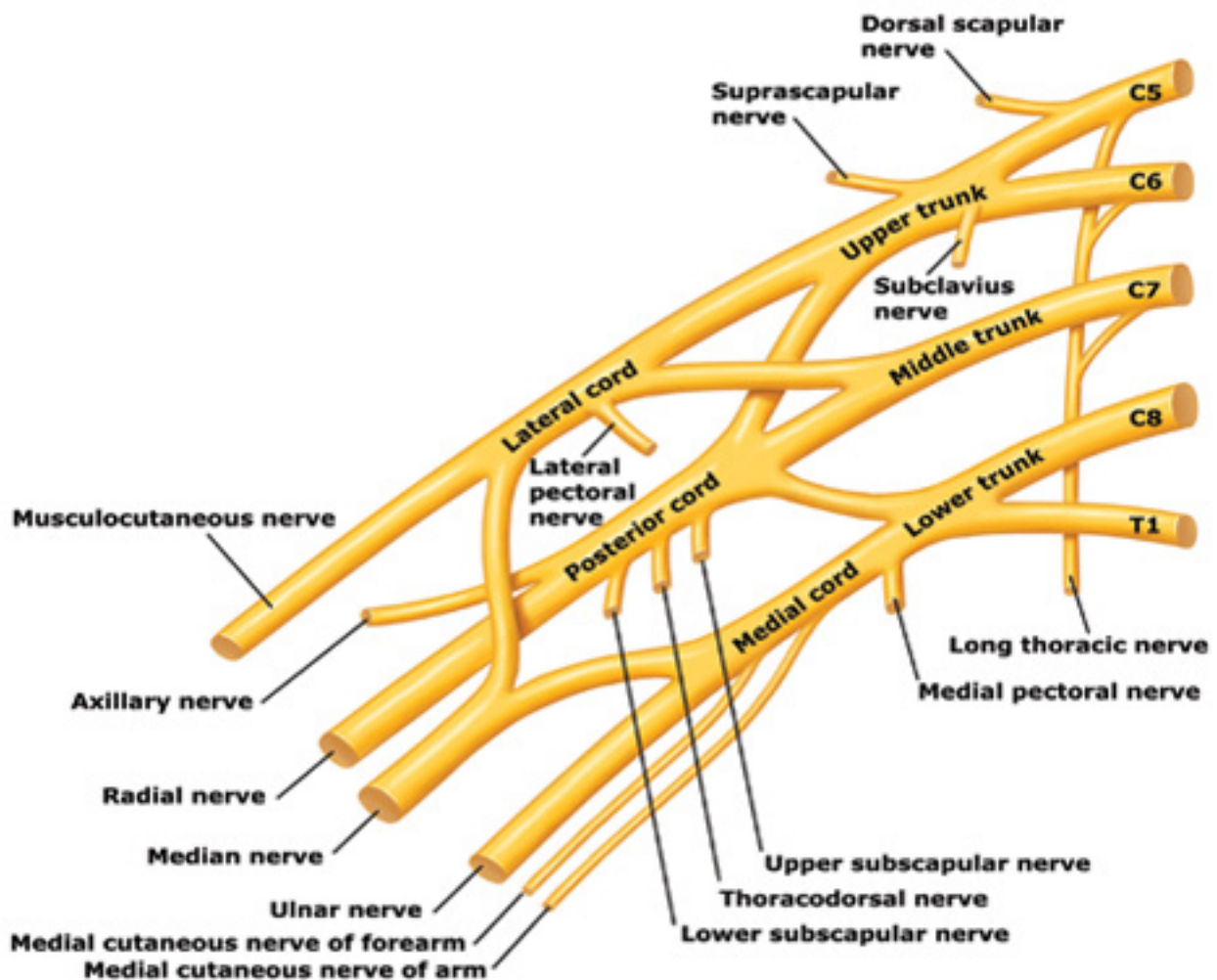


Figure 1: The Brachial Plexus⁸

2.3. Pharmacology of local anesthetics: Can local anesthetics cause sedation?

In 1885, William Halsted and Richard Hall of New York described and demonstrated the brachial plexus block using cocaine.⁹ As the use of cocaine grew, its alarming side effects became more evident, resulting in it losing favour in the medical world.⁹ Nils Lofgren, in 1943, developed and synthesised lignocaine.⁹ Its side effect profile was quickly established at the higher dose spectrum, and the ease of managing these, along with the protracted half-life, brought favour to its use in the medical field.⁹

The typical local anesthetic is a tertiary amine separated from an aromatic ring system by an intermediate chain. This chain contains either an ester or an amide linkage. (Figure 2) The aromatic ring end is a lipophilic end and the tertiary amine end is hydrophilic.¹⁰ Amides are much more stable molecules than the esters and are slowly metabolised in the liver.¹⁰

Bupivacaine was established in 1963.¹¹ The systemic distribution of bupivacaine follows the two-compartment model of pharmacokinetics, and it has a tendency to accumulate in highly perfused organs, of which the brain is one.¹⁰ Bupivacaine is metabolised in the liver via enzymatic breakdown. It undergoes N-dealkylation to a less toxic substance called pipercolylxyldine (PPX), which further undergoes hydroxylation and glucuronidation before being excreted by the kidneys.¹¹

A high concentration of bupivacaine has a relatively quick onset of action (0.5% versus 0.25%), and combined with its long duration of action, bupivacaine is therefore a better option over lignocaine for regional techniques.¹⁰ Bupivacaine also provides a more effective sensory than motor blockade when given via the epidural route at concentrations between 0.25% and 0.75%.¹⁰

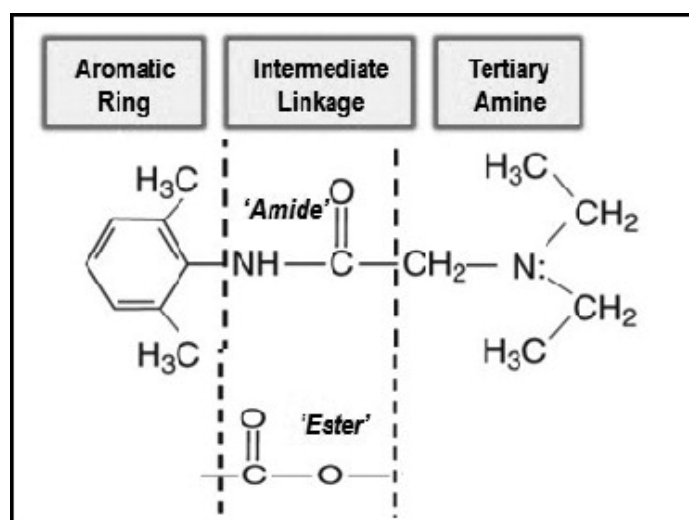


Figure 2: A schematic representation of the structure of local anesthetics¹²

Local anesthetics work by blocking voltage gated sodium channels, thereby preventing the initiation and propagation of an action potential along a nerve axon. Apart from inhibiting various receptors, they also reduce the release of glutamate¹³, and depress many intracellular signalling pathways.¹⁰ Due to these actions; one could postulate that, by preventing the development of an action potential, or by reducing the release of excitatory cerebral neurotransmitters, local anesthetics could cause sedation.

At clinically relevant doses, local anesthetics also affect potassium and calcium channels, which could possibly explain some of their pro-arrhythmia and pro-seizure side effects.¹⁴

2.4. Complications from peripheral nerve blocks

The complications of peripheral nerve blocks include peripheral nerve injury, bleeding, and local anesthetic systemic toxicity (LAST).¹⁵

The progressive improvement in the technique of performing nerve blocks, from initial anatomical landmark identification only, to eliciting paraesthesia with a nerve stimulator, to the eventual ultrasound- guided techniques, has reduced the rate of complications from nerve blocks.¹⁵

In a gigantic study with over 7000 study patients, undergoing an array of nerve blocks with nerve stimulator- assistance, ultrasound guidance or both, less than 0,5% of patients had suspected nerve injury requiring neurological assessment following the block. Of these patients, only 0,05% met the criteria for nerve injury related to peripheral nerve block.¹⁵ Though this study does not suggest that ultrasound guided is a safer means than nerve stimulator guided, it does emphasise that the risk for nerve injury is always there, though very rare.¹⁵

Local anesthetic systemic toxicity (LAST) remains a major source of morbidity and mortality from regional anesthesia. Symptoms range from and include¹⁵; auditory changes; metallic tastes; agitation; central nervous system changes, (including seizures and coma) and cardiovascular events, such as hypotension, hypertension, arrhythmias and cardiac arrest.¹⁵

Central nervous system symptoms of toxicity are usually excitatory, and thought to be related to a blockade of inhibitory pathways in the cerebral cortex.¹⁰ It has however been shown that when an unusually large dose of local anesthetic is administered, a depressive state can occur, that results from inhibition of both inhibitory and facilitatory neurotransmission.¹⁰ The inhibition of glutamate is thought to also play a role here.¹⁰ These depressive states are usually preceded by excitatory

phases. These central nervous system effects, though not entirely understood, could explain why, and how, local anesthetics might affect levels of consciousness.

In 2006, intralipid use was first documented in humans.¹⁵ The theory behind its effectiveness is that the lipid acts as a “sink”, drawing the local anesthetic into the fat layer.¹⁵ The lipid: aqueous partition coefficient of bupivacaine is 11.9, thus making this theory very favourable.¹⁵ Following the administration of local anesthetics, the onset of symptoms due to LAST tend to occur within the first few minutes. This is evident by the American Society of Regional Anesthesia’s recently published advisory, suggesting that anesthetists perform vigilant monitoring for at least 30 minutes after performing nerve blocks.³

2.5. Measurement of level of consciousness: BIS monitoring

Sedation includes spectrums of consciousness ranging between minimal sedation to general anesthesia. During sedation, the important variable for the doctor is the preservation of verbal contact with the patient whilst he or she is being sedated. The sedation of patients undergoing surgical procedures under loco-regional anesthesia is not standard code of practice, and is done according to the anesthesiologist’s preference.⁴ Sedation has many advantages for patients, including anxiolysis, reduced post-operative recall, and generally a better global tolerance to loco-regional anesthesia being performed.

Sedation, however, has been associated with many negative effects. In a large study involving some 17000 patients undergoing cataract surgery, a significant increase in adverse outcomes, particularly cardiovascular events, was noted when intravenous sedatives were used as opposed to no sedation. There is also an increased incidence of undiagnosed obstructive sleep apnoea becoming apparent in patients receiving procedural sedation.⁴

The electroencephalogram (EEG) signal reflects the electrical activity of the neurons in the cerebral cortex over time. It is the gold standard in assessment of the level of sedation or hypnosis. It is very sensitive to pharmacological and physiological changes, and its oscillatory nature makes it a good subject of mathematical analysis in measuring changes in levels of consciousness.¹⁶

The EEG tracing is a sum of the excitatory and inhibitory postsynaptic activities on the cortex. It measures potential differences predominantly from the pyramidal cells, which, in a quiet state, are synchronised with a slow wide complex; and when excited, are not synchronised with rapid

oscillations and low amplitude signals. EEG tracings offer the ease of visual analysis without the need for mathematical analysis.¹⁶ EEG analysis has advanced, allowing now for both time and frequency domain analysis.¹⁶

Frequency domain analysis allows a measure of mean signal amplitude, frequency and the burst suppression ratio (BSR), which represents the portion of time the EEG trace is flat. Spectral analysis is derived from Fast Fourier Transform. This separates a complex sinusoidal wave into a sum of simple waveforms of specific frequency and voltage. This allows for various numerical parameters to be deduced, including the spectral power of the different frequency bands (α , β , δ , θ).¹⁶ (Figure 3)

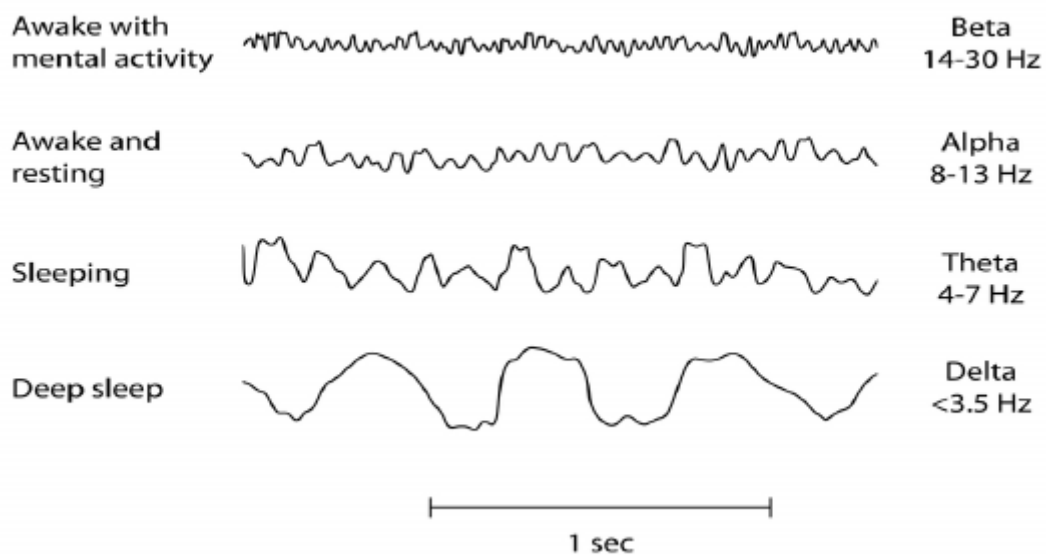


Figure 3: The EEG tracings¹⁷

Bispectral analysis is another spectrum of analysis within the frequency domain. It also uses Fast Fourier Transform, allowing a comparison to be made between 2 waves at a time, thus creating a third harmonic that measures the degree of synchronisation between the 2 waveforms. A degree of synchrony is calculated between the number of waveforms and the number of harmonics of the spectrum. Synchronisation increases with increasing depth of sedation and anesthesia. Consequently, one will find low frequency high amplitude waveforms with sedation and anesthesia.¹⁶

The variation of successive segments of the EEG may be described via mathematical models wherein the last segment may obey or diverge from the proposed model.¹⁶

When the signal follows the model, it is described as having high regularity, with good predictability. The complexity is thus described as being low. Should the individual segments differ from the proposed series, complexity will grow, while regularity and predictability will be reduced.¹⁶ With so many varying parameters to assess in a raw EEG, algorithms have been established to integrate the varying parameters. These included the development of more sophisticated monitors such as the bispectral index (BIS) monitor.¹⁶

BIS is calculated from 3 parameters: the spectral analysis, the bispectral analysis and the temporal analysis. It thus considers the beta ratio (the percentage of rapid beta frequencies measured by spectral analysis of the EEG), the degree of synchronisation and the burst suppression ratio. This makes BIS monitoring an effective means to assess sedation. The newer XP version of the BIS, which has 4 rather than the standard 3 electrode sensors, also measures and subtracts the effect of electromyography, which can also contribute to parts of the EEG.¹⁶

BIS Index is a dimensionless number scaled to clinical endpoints as well as specific EEG features. The scale is from 0 to 100. Deep to light sedation is considered between 60 to 90 and 90 to 100 is considered awake. This is demonstrated in figure 4.¹⁸

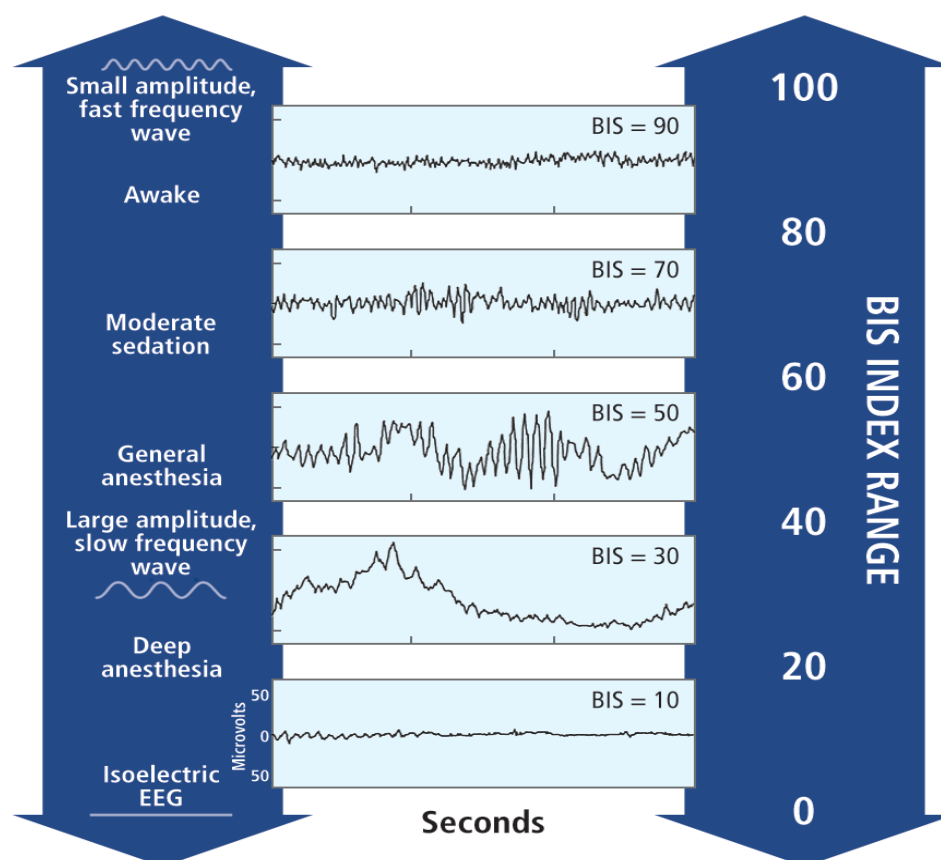


Figure 4: BIS value ranges¹⁹

In a review by Kent and Domino²⁰, the term ‘depth of anesthesia monitoring’ has been described as a misnomer, as they only monitor depth of sedation or hypnosis.²⁰ Deep general anesthesia has been documented to be associated with poor outcomes, including neurocognitive dysfunction and mortality, thus validating the use of ‘depth of anesthesia monitoring’, particularly in those with significant comorbidities.²⁰

Although there are many different monitors available for commercial use, BIS monitoring has the most literature evaluating its use. Twelve lead EEG monitoring remains the gold standard in cerebral monitoring.²⁰ Cottenceau et al.²¹ compared BIS and raw EEG monitoring in patients with severe brain injury with refractory intracranial hypertension. Cottenceau et al.²¹ concluded that the relationship between BIS and the suppression ratio from EEGs was well correlated in traumatic brain injured patients being treated with barbiturates in predicting a specific burst suppression pattern.²¹

Before the advent of processed electroencephalogram type monitors to assess the depth of sedation, monitoring sedation has been qualitative; involving observed clinical parameters such as physical appearance, response to vocal stimulus and pain in response to surgical stimulation. Such stimuli, namely vocal or painful stimuli, in themselves will alter the level of sedation, thus affecting the validity of such subjective sedation assessment means.⁵

2.6. Review of studies of neuraxial loco-regional anesthesia and the effect on level of consciousness and sedation

The effect of local anesthetic agents on sedation in patients receiving neuraxial anesthesia has been studied, and it has been well documented that neuraxial anesthesia with local anesthetic agents decreases the afferent stimulation of the reticular activating system via the spinothalamic afferent tracts.¹ This has been shown to reduce the dose of both intravenous and inhalational anesthetic agents needed to acquire a defined level of sedation. As far back as 1994, Tverskoy et al.²² demonstrated in a study with 53 ‘nonpremedicated’²² patients that subarachnoid (spinal) bupivacaine blockade decreased the hypnotic requirements for thiopentone and midazolam due to the reduced afferent input to the reticular activating system. Tverskoy et al.²² used loss of the ability to open eyes on verbal command as a measure of hypnotic endpoint.¹

Besides the blockade of afferent input via the spinothalamic tracts, two other theories have been considered to explain the altered levels of consciousness following neuraxial anesthesia with local

anesthetics. Firstly, there is the possibility of rostral spread of the local anesthetic, with direct action on the brain. In rat model studies, Eappen and Kissin (1998)¹ showed that despite intrathecal bupivacaine being associated with decreased general anesthetic requirements, there was no bupivacaine detectable in the actual brain or cervical spinal cord. This thus disproved the theory of local anesthetics directly affecting the brain.¹ Secondly, the systemic effects of local anesthesia have been considered. Pollock et al.¹ described studies by both Ingaki et al. (1994) and Tverskoy et al. (1996) which looked at the effect on sedation using epidural versus intravenous lignocaine and intramuscular versus epidural bupivacaine. They found that the epidural groups needed less sedation compared with the systemic groups, thus suggesting that the systemic levels of the local anesthetic might not contribute to the sedation associated with neuraxial blockade.¹

Quantifying the level of consciousness during spinal anesthesia had not been attempted until 2000, when Pollock et al.¹ attempted to quantify the levels of sedation induced by spinal anesthesia by using BIS monitoring and comparing these to Observer Assessments of Alertness/Sedation (OAA/S) scales (see figure 5) and the patient's self-sedation score of depth of sedation. Pollock et al.¹ found that 'un-premedicated spinal volunteers'¹, receiving spinal anesthesia had significant changes in consciousness as measured by OAA/S and self-sedations scores. In addition, they showed that a statistically significant drop from baseline BIS scores were noted in these patients; with the peak effect of sedation not related to the peak of spinal anesthesia, but rather occurring at 60 minutes after the spinal injection.¹

5. Responds readily to name spoken in normal tone
4. Lethargic response to name spoken in normal tone
3. Response only after name is called loudly and/or repeatedly
2. Response only after mild prodding or shaking
1. Response only after painful trapezius squeeze
0. No response after painful trapezius squeeze

Figure 5. The modified OAA/S responsive scale²³

3. Hypothesis, Outcomes

In this pilot study, our null hypothesis is that supraclavicular brachial plexus blocks do not alter levels of consciousness, as measured by BIS monitoring. The alternate hypothesis is that supraclavicular brachial plexus blocks alter levels of consciousness, as measured by BIS monitoring.

Our primary outcome was the effect of supraclavicular blocks on BIS in the hour following block placement. This was compared to control BIS readings obtained before the brachial block was performed. Our secondary outcome was to consider if the change in BIS was consistent with decreased levels of consciousness.

4. Methodology

Ethics approval was obtained from the Health and Research Ethics Committee of Stellenbosch University. (Ethics Reference #: S15/01/008)

Exclusion criteria included the following:

1. Patients fasted for >8 hours pre-operatively
2. Any patient with known allergies to the local anaesthetics
3. Any patients with clinical signs of pre-existing or undiagnosed peripheral neuropathy
4. Any patient with known contraindications to receiving a peripheral nerve block (including bleeding diatheses), or who developed complications from the peripheral nerve block
5. Any patient with known neurological or psychiatric illness or receiving any neuroleptic medication
6. Any patient who was anxious to a point requiring pharmacological sedation
7. Patients who have received narcotics, anxiolytics or analgesics in the preceding 12 hours
8. Patients below 18 or over 65 years of age
9. Patients whose blocks were patchy or were considered a 'failure'
10. Patients whose baseline oxygen saturation fell below $\leq 94\%$
11. Patients whose oxygen saturation decreased to $\leq 94\%$ after receiving the block
12. Patients whose blood pressure deviated by $\geq 20\%$ from baseline after receiving the block

The study took place in the orthopaedics theatres of Tygerberg Academic Hospital. During the pre-operative consultation, patients were counselled and offered either general anesthesia, or regional anesthesia by means of a supraclavicular brachial plexus block. Patients who opted for the loco-

regional technique were invited to participate in the study. Consent forms were available in English, Afrikaans and isiXhosa (Appendix A, B, C). Twenty American Society of Anesthesiology (ASA) class I patients undergoing elective upper limb surgery accepted the invitation to participate. Prior written, informed consent was obtained.

Regional blockade was performed in a quiet induction room adjacent to the operating theatre. In keeping with the methodology of Pollock and colleagues neuraxial anesthesia-sedation studies¹, the lights were dimmed and all data was collected before the surgery.

Intravenous access was secured before the block. Routine monitoring included non-invasive blood pressure monitoring, 3 lead electrocardiography, and pulse oximetry. Baseline physiological observations were obtained before the block was performed.

The patient completed a pre-block numerical Visual Analogue Score (VAS) to describe their current pain experience (0cm = no pain; 10cm = unbearable pain) (Appendix E). Thereafter, BIS electrodes were applied. A pre-block BIS control reading was acquired by placing the patient quietly in the dimmed induction room, and documenting the lowest BIS score over a 10minute interval.

The principal investigator performed the supraclavicular brachial plexus block. Using strict asepsis, the patient was positioned supine and the needle was placed using ultrasound guidance (NanoMaxxTM Ultrasound System, SonoSite, Inc. Bothell, WA 98021 USA). A 10-4 MHz linear ultrasound probe was used. The block was performed using a 50mm, 22gauge short bevel insulated nerve stimulator needle. Bupivacaine 0.5% was infiltrated into the block field at a dose of 2mg/kg. As the concomitant use of nerve stimulation and ultrasound assisted supraclavicular brachial plexus blocks makes minimal further contribution to limiting nerve injury, no nerve stimulation was employed.²⁴

Following the block, patients were monitored for local anaesthetic toxicity or other complications. Both ASRA and the New York School of Regional Anesthesia (NYSORA) suggest a minimum of 30minutes of vigilant monitoring after performing the block, in order to detect any regional anesthesia associated complications.^{25, 26} Each study patient received continuous monitoring of haemodynamics and overall wellbeing well beyond the study time of 60minutes, care for the patient

only ending after the surgical procedure. Should toxicity have developed, the ASRA local anaesthetic systemic toxicity treatment algorithm²⁵ would have been employed (Appendix G).

After block placement, the lowest BIS value for each 10minute interval was documented until the end of 60minutes post-block. This value was determined by visual inspection of the BIS variability by the principal investigator. All BIS data was collected pre-operatively in the block room.

Statistical analysis

Mr Michael McCaul, a consultant at the Biostatistics Unit within the Centre for Evidence Based Health Care (CEHBC), Stellenbosch University, assisted with the analysis of this pilot study. Funding for this Unit is via support from the Dean's Fund of the Faculty of Medicine and Health Sciences, Stellenbosch University.

As no previous studies specifically investigated effects of any non-neuraxial loco-regional anesthesia on BIS, we were unable to do a power analysis using data from previous studies.

Consequently, a convenient sample size was chosen.

Statistical significance was considered at $p < 0.05$. Data was collected in a Microsoft Excel© spreadsheet and was analysed using Stata ® 14.

Continuous variables (changes in BIS) that were normally distributed were analysed with means and standard deviations, with 95% confidence intervals used to estimate population means.

Categorical variables were analysed using frequency distributions presenting the absolute and relative frequencies and 95% confidence intervals for binary proportions were used to estimate population proportions. When comparing two continuous or ordinal variables, Pearson correlations were used for data that was normally distributed. When comparing a binary variable that represents dependent groups or measurements over time (changes in BIS at each observation interval) a dependent samples T-test was performed.

Data preservation is in accordance with the guidelines set out by the South African Good Clinical Practice (SAGCP) 2006 guidelines.²⁷

5. Results

Twenty patients were enrolled in the study. All 20 patients had successful blocks and none required further analgesia for performance of their surgery.

No complications from the blocks were detected.

Sample No:	Pre-op Pain score (cm)	Age (years)	Sex	Nature of illness	Pre-op BIS Scores	Lowest BIS obtained in 60minutes
1	0	48	male	chronic	97	78
2	0	18	female	trauma	96	38
3	0,5	21	male	trauma	95	57
4	5,8	27	female	chronic	95	77
5	5,9	21	male	trauma	97	78
6	0	32	male	trauma	98	91
7	3,5	39	male	trauma	97	83
8	0	36	male	trauma	98	67
9	0,5	25	male	trauma	98	74
10	8	43	female	trauma	94	80
11	2	21	female	trauma	98	74
12	2,9	18	female	trauma	98	92
13	0	25	male	trauma	98	58
14	5,1	33	male	trauma	97	73
15	0	26	male	trauma	98	91
16	4,1	40	male	chronic	94	63
17	5,9	42	male	trauma	98	88
18	0	19	male	trauma	98	87
19	4,8	37	male	trauma	97	89
20	0	31	male	trauma	98	58

Table 1: Sample demographics and results

Patient demographics are presented in table 1. The mean age of the sample population was 30.1 ± 9.30 years (95% CI of 26.02 to 34.18).

5 (25%) were female and 15 (75%) were male.

Indications for the upper limb surgery were traumatic or chronic, pre-existing conditions (e.g., carpal tunnel syndrome) in 85% and 15% of study patients respectively.

Median pre-operative pain scores were 1.25 (Interquartile range 0 to 4.95) with a mean value of 2.45 ± 2.69727 (95% CI of 1.27 to 3.63).

‘Control’ pre-block BIS values:

The mean control pre-block BIS value was 96.95 ± 1.40 (95% CI 96.34 to 97.56). The lowest pre-block BIS value was 94.

Effect on BIS readings during the 60minute observation period post block:

Thirteen (65%) (95% CI 40.4% to 83.6%) patients demonstrated a decrease in $BIS \leq 80$ at some time during the 60minute post block observation period. Six (30%) and 4 (20%) patients demonstrated a decrease in BIS to less than 70 and 60 respectively. The lowest reduction in BIS occurred during the 5th 10minute observation period with 50% of patients demonstrating $BIS \leq 80$ at this observation period (95% CI 27.68% to 72.32%).

The mean drop in BIS readings observed after the block, during the 6 ten minute observation periods were 74.8 ± 14.34 (95% CI 68.52 to 81.08).

Relationship between preoperative pain scores and drop in BIS:

The mean pre-block pain scores between the patients who demonstrated a drop in $BIS \leq 80$ during the 6 ten minute observation periods versus those who had a $BIS > 80$ were 2.45 ± 2.91 (IQR 0 to 5.1) (95% CI of 1.18 to 3.73) and 2.44 ± 2.47 (IQR 0 to 4.8) (95% CI of 1.36 to 3.53) respectively (two-sample Wilcoxon rank-sum test, $p = 0.9022$).

Effect on BIS due to age:

There was a negative correlation between pre-block control BIS values and age ($r < -0.23$, $p = 0.318$). At each 10minute observation interval after the block, there was a positive correlation between increasing age and a decrease in $BIS \leq 80$, although this was not statistically significant ($p > 0.05$).

Effect on BIS due to gender:

The BIS nadir for both genders occurred at the 5th ten minute interval. No gender related differences in the lowest BIS values occurred (males and females 75.4 ± 21.68 (95% CI of 56.4 to 94.4) and 79.53 ± 13.32 (95% CI of 72.79 to 86.27) respectively (t-test= -0.514, p=0.613).

Relationship between the drop in BIS and the reason for the surgery:

A $BIS \leq 80$ was observed in 58.82% and 100% of patients with trauma and pre-existing chronic conditions respectively within the 60minute observation period (p=0.521).

6. Discussion

We conducted a pilot study to investigate the effect of non-neuraxial loco-regional anesthesia (supraclavicular brachial plexus blockade) on Bispectral index (BIS). In the 60minute observation period following the supraclavicular brachial plexus block using 2mg/kg of 0,5% bupivacaine, 65% (CI⁹⁵ 40.4% 83.6%) of individuals exhibited a $BIS \leq 80$ over the next 60 minutes.

The BIS declined to a nadir of 74.8 ± 14.34 (95% CI 68.52 to 81.08) during the hour after the block. Pre-existing pain scores, pre-existing conditions, age, and gender did not affect the decline in BIS.

The null hypothesis is rejected and the alternate hypothesis that supraclavicular brachial plexus blocks do alter levels of consciousness, as measured by BIS monitoring, is accepted.

BIS as a tool to measure sedation:

BIS monitoring is an effective means to assess sedation. It is calculated from 3 parameters, namely the spectral analysis, the bispectral analysis and the temporal analysis and it considers the beta ratio (the percentage of rapid beta frequencies measured by spectral analysis of the EEG), the degree of synchronisation and the burst suppression ratio. The relationship between BIS and the suppression ratio from EEG monitoring (The gold standard for monitoring sedation²⁰) has been well correlated.²¹

The effects of neuraxial anesthesia on BIS:

The effect of neuraxial regional anaesthesia on BIS has been well demonstrated by Pollock et al when they demonstrated a statistically significant drop from baseline BIS values in patients following spinal anaesthesia techniques.¹ Decreased afferent stimulation via the spinothalamic tracts into the reticular activating system has been the most plausible theory, described as far back

as 1994 by Tverskoy,¹ although the possibility for rostral spread of the local anaesthesia in the central neuraxis, or the possibility that the local anaesthesia could have a systemic effect have not been clinically excluded.

The effects of neuraxial anesthesia on Sedation scores:

The altered states of consciousness induced by neuraxial regional anesthesia has also been demonstrated by Pollock et al by means of Observer Assessments of Alertness/Sedation (OAA/S) scores, where significant changes were also demonstrated, indicating that neuraxial regional anaesthesia can decrease levels of consciousness, and this decrease can be found in more than one measurement tool (Bispectral index monitors and Observer Assessments of Alertness/Sedation (OAA/S) scores)

Why could loco-regional anesthesia be associated with a decrease in BIS?

- a) Following neuraxial anesthesia, lowered levels of consciousness may be because of rostral spread of the local anaesthetic to the brain.¹ In non-neuraxial loco-regional anaesthesia however, local anaesthetics are not usually able to directly spread to the central nervous system. The decrease in BIS we observed therefore supports Eappen and Kissen¹ murine studies, in which no bupivacaine was detected in animal brains after subarachnoid blocks.
- b) It is thought that sedation with neuraxial regional anesthesia is induced by directly reducing the sensory input into the brain by blocking the afferent spinothalamic tracts.¹ This is certainly a plausible causal theory for sedation in patients who have had non-neuraxial loco-regional anesthesia. Though there is no direct blockade of spinothalamic tracts in non-neuraxial loco-regional anesthesia techniques, the blockade of afferent peripheral nerves reduces facilitatory input into the reticular activating system, thereby contributing to sedation.²⁸
- c) A comparison can be drawn between a noisy environment being silenced and the ‘noise’ of peripheral tactile sensation being silenced by non-neuraxial loco-regional anesthesia. By blocking out a percentage of the peripheral sensory input with a non-neuraxial loco-regional technique, the brain has less total sensory input to process. With less sensory input (“noise”), the patient is likely to feel more “sleepy” (more sedated).
- d) Such a theory could be used to describe Ozkan-Seyhan’s²⁸ findings that a higher level of spinal anesthesia was related to a lower consumption of propofol used for sedation when compared to lower level of spinal anesthesia.²⁸ In other words, a higher level of spinal anesthesia caused a greater reduction in the percentage of sensory input (“noise”) to the

central nervous system, with an enhanced sedative effect. Nishikawa et al.²⁹ noted that high spinal blockade (to the level of the sixth thoracic space and above), may significantly reduce BIS values ($p < 0.001$), without an associated reduction in regional cerebral oxygen saturation, while low spinal blockade (below the twelfth thoracic space) had no effect on BIS values ($p < 0.001$).²⁹

- e) Studies have shown that patients with chronic spinal cord injury require reduced amounts of thiopental for induction of anesthesia and tracheal intubation versus able-bodied patients.³⁰ This is a further testament to the theory that sedative states appear to be enhanced when the total number of sensory inputs into the cortex of the brain are reduced.

The effect of sex on drop in BIS:

There was no statistically significant difference between the change in mean BIS values between males and females. The female patients however obtained a lower BIS (75.4 ± 21.68) than the male patients (79.53 ± 13.32).

The effect of pre-block pain score on drop in BIS:

It appeared that patients with the least amount of pre-block pain had a greater incidence of sedation. ($BIS \leq 80$), but this was statistically insignificant ($p > 0.05$). This was surprising as one would expect that the relief of pain would increase relaxation and sedation.

Timing of peak incidence of drop in BIS:

Pollock demonstrated that maximal sedation was not experienced at the peak of the neuraxial loco-regional anesthesia, but at roughly 60 minutes after the blockade was initiated. In this study, non-neuraxial loco-regional anesthesia had similar finding, with the maximal incidence of a $BIS \leq 80$ occurring at around the 50minute interval. In 1976, Moore et al demonstrated that following supraclavicular brachial plexus block, the mean peak arterial and venous plasma concentrations of bupivacaine occurred between 30-35minutes after the block at a concentration of 1.7 (range 1.05 to 2.40)mcg/ml and 1.55 (range 0.94 to 2.25) respectively.³¹

Strengths of this pilot study include:

1. There was no deviation from standard care offered to patients undergoing upper limb orthopaedic surgery. The application of the BIS monitor and the 60minute observation was the only added non-routine practice.

2. The long half-life of supraclavicular brachial plexus blocks with bupivacaine meant that the study could be performed before the surgery commenced, while the block remained effective long after the duration of the surgery, offering the patients good post-operative analgesia.

Limitations within this pilot study include:

1. The limited sample size impacted on the level of confidence with which these results can be interpreted.
2. In order to obtain a result with greater statistical confidence, (with a 10% precision within a 95% confidence interval), a sample size of 88 patients would be needed.
3. Each study patient consumed a minimum of 90 minutes of time, from counselling for consent, to detaching monitors and transferring to the operating room. Our health system is stricken with high patient volumes, limited operating time and demands for rapid patient turnover. Two patient data sets were obtained each week of this study, which would mean that a total of 44 weeks would be needed to obtain an adequately powered sample size.
4. Another possible limitation was that the induction room was a quiet and poorly lit environment. Though it was in line with the environment created by Pollock when he performed his observations on patients with neuraxial anesthesia¹, bias can be argued. Ozkan-Seyhan et al²⁸ argued that even Pollock's study might be flawed in that anyone could fall asleep in a quiet environment. Perhaps a reasonable approach would be to either have 2 patients in the room, one with a loco-regional anaesthetic and the other without and to observe BIS values over an hour on each; or to consider keeping the study patient for an hour before performing the loco-regional block and observing the lowest BIS within that hour. This would eliminate the effect of the environment on sedation, but would consume a further 60minutes in a time-limited environment.
5. Only one measurement tool was used, in the form of a BIS monitor. Due to only one observer being used to document BIS values, it would have been technically difficult for an Observer Assessments of Alertness/Sedation (OAA/S) score to be simultaneously done. Such a qualitative assessment of sedation would have also required assessing response to vocal stimulus and pain in response to stimulation, which in itself could alter the level of sedation⁵, and could thus impact on the BIS readings obtained within the data set.

7. Conclusion

We conducted a pilot study to investigate the effect of non-neuraxial loco-regional anesthesia (supraclavicular brachial plexus blockade) on BIS. Following informed consent, 20 patients scheduled for hand surgery agreed to be enrolled into the study. Without premedication, sedation, additional analgesia or complications, we successfully administered ultrasound guided brachial blocks to all enrolled patients. The mean control pre-block BIS value was 96.95 ± 1.40 (95% CI 96.34 to 97.56).

Following supraclavicular brachial plexus block using 2mg/kg of 0,5% bupivacaine, 65% (CI⁹⁵ 40.4%-83.6%) of individuals exhibited a BIS ≤ 80 over the next 60 minutes. The mean drop in BIS readings observed after the block, during the 6 ten minute observation periods were 74.8 ± 14.34 (95% CI 68.52 to 81.08).

It appears that supraclavicular brachial plexus blocks do decrease BIS values to a level consistent with light to moderate sedation. The null hypothesis is rejected and the alternate hypothesis that supraclavicular brachial plexus blocks do alter levels of consciousness, as measured by BIS monitoring, is accepted.

These findings justify a formal, larger study of 88 patients to formally investigate the effect of non-neuraxial loco-regional anesthesia techniques on BIS. Further information supporting a relationship between local anaesthetic drugs, loco-regional techniques (neuraxial and non-neuraxial) and altered levels of consciousness, might bring us closer to establishing a pharmacological or physiological pathway linking these together.

8. References

1. Pollock JE, Neal JM, Liu SS, Burkhead D, Polissar N. Sedation during spinal anesthesia. *Anesthesiology*. 2000 Sep; 93(3): 728-734.
2. Antognini JF, Jinks SL, Atherley R, Clayton C, Carstens E. Spinal anaesthesia indirectly depresses cortical activity associated with electrical stimulation of the reticular formation. *Br J Anaesth*. 2003 Aug; 91(2): 233-238. DOI: 10.1093/bja/aeg168
3. Morley AP, Chung DC, Wong AS, Short TG. The sedative and electroencephalographic effects of regional anaesthesia. *Anaesthesia*. 2000 Sep; 55(9): 864-869.
4. Hohener D, Blumenthal S, Borgeat A. Sedation and regional anaesthesia in the adult patient. *Br J Anaesth*. 2008 Jan; 100(1): 8-16. DOI:10.1093/bja/aem342
5. Khurana P, Agarwal A, Verma R, Gupta P. Comparison of Midazolam and Propofol for BIS-Guided Sedation During Regional Anaesthesia. *Indian J Anaesth*. 2009 Dec; 53(6): 662-666.
6. Cobbold A, Money T. Regional anaesthesia: back to basics. *The Journal of Perioperative Practice*. 2010 Aug; 20(8): 288-293.
7. Rasool F, Bartsch A, Ahmed A, Gaur A. Ultrasound-guided Supraclavicular Brachial Plexus Block. *International Journal of Ultrasound and Applied Technologies in Perioperative Care, IJUTPC*. 2010 January-April; 1(1): 39-48.
8. Barbieri RL. The natural history of obstetric brachial plexus injury. Frontline Medical Communications Inc., Parsippany, NJ, USA. [Updated 2013 Feb; cited 2015 Jan 02]. Available from: www.obgmanagement.com/home/article/the-natural-history-of-obstetric-brachial-plexus-injury/3bc016afbf8b15ddd6c4a145bfe43e8a.html.
9. Wildsmith T. Principles and Practice of Regional Anaesthesia (4 ed.). Oxford University Press. 2012. Part 1, Chapter 1. History and development of local anaesthesia. [cited on January 2, 2014] Available on <http://oxfordmedicine.com/view/10.1093/med/9780199586691.001.0001/med-9780199586691-chapter-001>.
10. Miller RD. Miller's anesthesia. 6th ed. Edinburgh: Churchill Livingstone; 2004.
11. Gantenbein M, Attolini L, Bruguerolle B, Villard PH, Puyou F, Durand A, Lacarelle B, Hardwigsen J, Le-Treut YP. Oxidative metabolism of bupivacaine into pipecolylxylidine in humans is mainly catalyzed by CYP3A. *Drug Metab Dispos*. 2000 Apr; 28(4): 383-5.
12. Becker DE; Reed KL. Local Anesthetics: Review of Pharmacological. American Dental Society of Anesthesiology. [Cited on 7 September 2016] Available at:

https://adsa.cdeworld.com/courses/20191-Local_Anesthetics:Review_of_Pharmacological_Considerations#sthash.TC5dxV8Q.dpuf

13. Lin T.Y, Chung C.Y, Lu C.W, Huang, S.K, Shieh, J.S, Wang, S.J. Local anesthetics inhibit glutamate release from rat cerebral cortex synaptosomes. *Synapse*. 2013; 67: 568-579. doi:10.1002/syn.21661 5
14. Scholz A. Mechanisms of (local) anaesthetics on voltage-gated sodium and other ion channels. *Br J Anaesth*. 2002 Jul; 89(1): 52-61.
15. Jeng C, Torrillo T, Rosenblatt M. Complications of peripheral nerve blocks. *Br J Anaesth*. 2010; 105(S1): i97-i107.
16. Constant I, Sabourdin N. The EEG signal: a window on the cortical brain activity. *Paediatr Anaesth*. 2012 Jun; 22(6): 539-552.
17. Abhang PA, Gawali BW. Correlation of EEG Images and Speech Signals for Emotion Analysis. 2015, 10(5): page 4. DOI: 10.9734/BJAST/2015/19000
18. Agrawal D, Feldman HA, Krauss B, MD, Waltzman ML. Bispectral Index Monitoring Quantifies Depth of Sedation During Emergency Department Procedural Sedation and Analgesia in Children. *Ann. Emerg. Med.* (2004) 43:2 Page 2 4 8
19. Kelley SD. Monitoring Consciousness, USING THE BISPECTRAL INDEX™ (BIS™) DURING ANESTHESIA, A Pocket Guide for Clinicians, The BIS™ Index—A Continuum. Boulder, USA. COVIDIEN 2012. [Cited on 07 September 2016] Available from:
<http://www.covidien.com/imageServer.aspx/doc252087.pdf?contentID=77508&contenttype=application/pdf>
20. Kent CD, Domino KB. Depth of anesthesia. *Curr Opin Anaesthesiol*. 2009 Dec; 22(6): 782-787.
21. Cottenceau V, Petit L, Masson F, Guehl D, Asselineau J, Cochard JF, et al. The use of bispectral index to monitor barbiturate coma in severely brain-injured patients with refractory intracranial hypertension. *Anesth Analg*. 2008 Nov; 107(5): 1676-1682.
22. Tverskoy M, Shagal M, Finger J, Kissin I. Subarachnoid bupivacaine blockade decreases midazolam and thiopental hypnotic requirements. *J Clin Anesth*. 1994 Nov-Dec; 6(6): 487-490.
23. Coetzee, JF. Letter to the editor: Keeping the score. *SAfr J Anesthesiol Analg*. 2010; 16(4)
24. Togioka BM, Wu C. Supraclavicular Block. 2014; [cited 17 March 2014] Available from: <https://www.asra.com/pain-resource/article/44/supraclavicular-block>

25. Neal JM, Bernard CM, Butterworth JF, Di Gregorio G, Drasner K, Hejtmanck MR, Mulroy MF, Rosenquist RW, Weinberg GL. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med* 2010; 35: 152-161. [Updated 2012 Jan; Cited 2015 Apr 10]. <https://www.asra.com/advisory-guidelines/article/3/checklist-for-treatment-of-local-anesthetic-systemic-toxicity>.
26. Dewaele S, Santos AC. Toxicity of Local Anesthetics. NYSORA. New York. [Updated 2013 Sept 05; cited 2015 April 10]. Available from: <http://nysora.com/regional-anesthesia/foundations-of-ra/3075-toxicity-of-local-anesthetics.html>.
27. Department of Health. Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa, 2nd ed. Pretoria: Department of Health; 2006
28. Ozkan-Seyhan T, Sungur MO, Senturk E, Karadeniz M, Basel A, Senturk M, et al. BIS guided sedation with propofol during spinal anaesthesia: influence of anaesthetic level on sedation requirement. *Br J Anaesth*. 2006 May; 96(5): 645-649.
29. Nishikawa K, Hagiwara R, Nakamura K, Ishizeki J, Kubo K, Saito S, et al. The effects of the extent of spinal block on the BIS score and regional cerebral oxygen saturation in elderly patients: A prospective, randomized, and double-blinded study. *J Clin Monit Comput*. 2007 Apr; 21(2): 109-114.
30. Yoo, KY, Jeong CW, Jeong HJ, Lee SH, Na JH, Kim S, Jeong ST, Lee J. Thiopental dose requirements for induction of anaesthesia and subsequent endotracheal intubation in patients with complete spinal cord injuries. *Acta Anaesthesiol Scand* 2012; 56: 770–776
31. Moore DC, Mather LE, Bridenbaugh LD, Blafour RI, Lysons DF, Horton WG. Arterial and venous plasma levels of Bupivacaine following peripheral nerve blocks. *Anesth Analg*. 1976 Nov-Dec; 55(6): 763-768

9. Addenda

Appendix A: Patient Information leaflet and consent form

Title of research project: A pilot study to determine whether supraclavicular brachial plexus blocks using 0.5% bupivacaine decreases level of consciousness as measured by bispectral index (BIS)

Ethics committee reference number: S15/01/008

Principal investigator: Dr Rubendren Naidoo

Address: Department of Anesthesiology and Critical Care, Stellenbosch University,
Tygerberg Academic Hospital, Fransie Van Zijl Avenue, Tygerberg, 7505

Telephone numbers: +27836555934 / +2721 9385142

Email: placebo515@yahoo.com

Patient name:

Folder no.:

D.O.B:

(can place patient sticker here)

Introduction to a research Project: Your rights and responsibilities

You are being invited to take part in a research project.

Please take some time to read the information presented here, which will explain the details about this project. Please ask the doctor any questions about any part of this project that you do not fully understand. It is very important that you clearly understand what this research entails and how you could be involved.

Your participation is entirely voluntary and you are free to decline to participate.

If you say no, the decision will not affect you negatively in any way whatsoever. You are free to withdraw from the study at any point, even if you initially agree to participate.

This study has been approved by the Committee for Human Research at

Stellenbosch University and will be conducted according to the ethical guidelines and principles of

the International Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research project all about?

Often, instead of making you completely asleep, and making you breathe with machines for simple arm operations, we only numb the nerves that provide feeling to the arm, while you remain awake. We do this by injecting numbing medication called “local anesthetics” around a group of nerves in your shoulder, which makes your entire arm numb. We do this often and this technique is well recognized. The nerves in the arm will be temporarily unable to experience any feeling or movement for between 6 and 12 hours.

We have noticed that this type of anesthetic allows for patients to go home sooner after their operations, and that they have better pain control long after the actual operation. This also means that the anesthetist (the doctor that performs the injection) does not have to use artificial breathing and life support during simple surgical procedures. By blocking these nerves, we also need to use less drugs like morphine, which affects how the lung and heart work (decreases your breathing and your blood pressure).

We have noticed that in other parts of the body, when this numbing medication is injected, such as in women giving birth who get “epidurals” for labour pain, the numbing medication takes the pain away so well, that the patients become a bit sleepy.

We want to see if the injection in your shoulder with this numbing medication also has a similar effect of causing you to become sleepy.

Why have you been invited to participate?

You are booked for an operation on your arm. You therefore need some form of “anesthetic”. Your anesthetist has advised you that you can either be “put to sleep” or you can have an injection in the shoulder to numb your nerves to the arm. You have chosen to have the injection, and therefore we are inviting you now to be part of this study. All your participation requires is that, before we do the injection in your shoulder, we place stickers on your forehead, which are connected to a machine that measures “sleepiness”. We will do nothing differently from how we normally give this injection into the shoulder to numb the nerves except we will monitor how awake you are before the injection and compare it to your “sleepiness” after the injection. We will do this for an hour before the actual operation. From the time you arrive in theatre until the operation is complete, either

myself or my colleague will remain with you to ensure you are comfortable and safe. We will do this by monitoring as we would for any patient receiving any anesthetic, checking your pulse and blood pressure.

Are there any risks involved in taking part in this project?

There are no extra risks to you as a result of your taking part in this study.

However, whenever the injection into the shoulder is done, there are some risks that we are well aware of and always take care to avoid.

Some of the risks associated with this procedure include:

- risk for receiving too much of the numbing medication. The name of the numbing medication is called bupivacaine. If too much is received, or if it is accidentally injected directly into a blood vessel, it can affect the heart and/or the brain. It can cause the heart to beat in a strange way and possibly could make the heart stop. It could also cause you to have strange feelings in your entire body and even the mouth, and could result in fits/seizures. We avoid this risk by accurately calculating the dose we need for your body size and by being very sure not to inject the medicine into the blood but just around the nerves. Should you experience any of the symptoms, we have all the necessary medication to fix these side effects that can occur.
- risk of accidentally puncturing your lung while the injection is being done. The risk of this occurring is very low, but, should this occur, it can easily be treated.
- risk of injecting the medication into, instead of around, the nerve. This can result in abnormal feelings of pins and needles; which usually goes away in 6 weeks. By having you awake while doing the injection, you will help by telling us if there are any sudden sharp pains, which is a good guide to whether we are too close to the nerves. We use an ultrasound when doing the injection, which helps a lot to ensure that we are injecting precisely in the area around the nerves.

Should you experience any of these symptoms or have numbness for an unusually long time, you can contact Dr Rubendren Naidoo, the study doctor at the contact details above.

These risks are associated with the injection in the shoulder itself. The only different thing that we would be doing in this study is to measure your “sleepiness” with the stickers on your forehead.

Again, there are no extra risks to you as a result of you agreeing to take part in the study.

We will be monitoring you all the time and if any of the risks mentioned above happens, we will do the necessary to help you.

In the case of any complication occurring, there are guidelines and rules that are used to assess the situation. These guidelines are called the South African Good Clinical Practice (SAGCP) 2006 guidelines, which are a set of rules regarding research on patients, and are approved and regulated by the Minister of Health. Section 4.11 of these guidelines specifically talk about compensation should any serious permanent injury occur. The chance of having a complication is rare, but should this happen and cause permanent injury, we will follow these guidelines set out to ensure you are appropriately compensated and safe. These guidelines, along with the health research committee, require that if you take part in this study, you will be covered by insurance, which the University of Stellenbosch has.

Who will have access to your medical records and files?

All information that will be collected will be treated confidentially. In the case where we publish the study in a journal for others to learn, your details will not be put into the journal article. Your details will remain anonymous. Only the study doctors involved in this project will have access to your information, which will be safely kept in accordance with guidelines set out by section 6.5 of the South African Good Clinical Practice (SAGCP) 2006 guidelines, which are a set of rules regarding research on patients, and are approved and regulated by the Minister of Health. Occasionally, the ethics committee who guides the research that is done at the University of Stellenbosch, will do an inspection to ensure that our study is safe, and they might also request access to your information. The contact details of the ethics committee are attached below in case you would like to ask them questions.

Will you be paid to participate in the study? Will you have any costs involved?

You will not be paid to take part in the study. There will be no costs involved for you, if you do take part.

If you have any questions, you can contact:

Dr Rubendren Naidoo, the study doctor at the contact details above.

If you have any concerns or complaints that have not been adequately addressed by your study doctor, please contact the Committee for Human Research at 021-938 9820.

Declaration by the patient

By signing below, I, _____ agree to take part in a research study entitled:

“A pilot study to determine whether supraclavicular brachial plexus blocks using 0.5% bupivacaine decreases level of consciousness as measured by bispectral index spectrophotometry (BIS)”

I declare that:

- I have read or had read to me this information and consent form.
- It is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.

Signed at (*place*) on (*date*)

.....

Signature of participant

.....

Signature of witness

Declaration by investigator

I (*name*) declare that:

- I explained the information in this document to
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*)

Signed at (*place*) on (*date*)

.....

Signature of investigator

.....

Signature of witness

Declaration by interpreter

I (*name*) declare that:

- I assisted the investigator (*name*) to explain the information in this document to (*name of participant*) using the language medium of Afrikaans/Xhosa.
- We encouraged him/her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her questions satisfactorily answered.

Signed at (*place*) on (*date*)

.....
Signature of interpreter

.....
Signature of witness

Appendix B: Informed consent translated into Afrikaans

DEELNEMERINLIGTINGSBLAD EN -TOESTEMMINGSVORM

TITEL VAN DIE NAVORSINGSPROJEK: 'n Proefstudie om te bepaal of supraklavikulêre blokke van die brachiale plexus met 0.5% bupivacaïne die bewussynsvlak, soos gemeet deur middel van bispektrale indeks (BIS), verlaag

VERWYSINGSNOMMER: S15/01/008

HOOFNAVORSER: Dr Rubendren Naidoo

ADRES: Departement Anesthesiologie en Kritieke Sorg, Universiteit Stellenbosch,
Tygerberg Akademiese Hospitaal, Francie van Zijl-rylaan, Tygerberg 7505

KONTAKNOMMER: +27836555934 / +2721 9385142 placebo515@yahoo.com

Naam van pasiënt:

Lêernommer:

Geboortedatum:

(Kan pasiëntplakker hier plak)

Inleiding tot 'n navorsingsprojek: U regte en verantwoordelikhede

U word genooi om deel te neem aan 'n navorsingsprojek. Lees asseblief hierdie inligtingsblad op u tyd deur aangesien die detail van die navorsingsprojek daarin verduidelik word. Indien daar enige deel van die navorsingsprojek is wat u nie ten volle verstaan nie, is u welkom om die navorsingspersoneel of dokter daaroor uit te vra. Dit is baie belangrik dat u ten volle moet verstaan wat die navorsingsprojek behels en hoe u daarby betrokke kan wees. U deelname is ook volkome vrywillig en dit staan u vry om deelname te weier. U sal op geen wyse hoegenaamd negatief beïnvloed word indien u sou weier om deel te neem nie. U mag ook te eniger tyd aan die navorsingsprojek onttrek, selfs al het u ingestem om deel te neem.

Hierdie navorsingsprojek is deur die Gesondheidsnavorsingsetiekkomitee (GNEK) van die Universiteit Stellenbosch goedgekeur en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki en die Etiese Riglyne vir Navorsing van die Mediese Navorsingsraad (MNR).

Wat behels hierdie navorsingsprojek?

Vir eenvoudige armoperasies laat ons u dikwels wakker bly terwyl ons net die senuwees verdoof wat gevoel aan die arm gee, in plaas daarvan om u heeltemal aan die slaap te maak en met masjiene te laat asemhaal. Ons doen dit deur 'n verdowingsmiddel wat “lokale verdowing” genoem word om 'n groep senuwees in jou skouer in te spuit, wat u hele arm verdoof. Dit is 'n goed erkende tegniek en ons doen dit dikwels. Die senuwees in die arm sal tydelik, vir tussen 6 en 12 uur, geen gevoel hê nie en ook nie kan beweeg nie.

Ons het opgemerk dat hierdie soort narkose pasiënte in staat stel om na hul operasies gouer huis toe te gaan, en dat hulle lank na die operasie self beter pynbeheer het. Dit beteken ook dat die narkotiseur (die dokter wat die inspuiting toedien) nie kunsmatige asemhalings- en lewensondersteuning tydens eenvoudige chirurgiese prosedures hoef te gebruik nie. Deur hierdie senuwees te blok, hoef ons ook minder middels soos morfien te gebruik, wat die werking van die longe en hart beïnvloed (jou asemhaling en bloeddruk verlaag).

Ons het opgemerk dat wanneer hierdie verdowingsmiddel in ander dele van die liggaam ingespuut word – soos met vroue wat geboorte skenk wat 'n “epiduraal” vir kraampyne kry – die verdowingsmiddel die pyn so goed blok dat pasiënte slaperig word.

Ons wil sien of die inspuiting met hierdie verdowingsmiddel in u skouer 'n soortgelyke uitwerking het, met ander woorde dat u slaperig word.

Waarom is u genooi om deel te neem?

U is vir 'n operasie aan u arm geskeduleer. U het dus 'n soort “narkose” nodig. U narkotiseur het u ingelig dat u óf “aan die slaap gemaak” kan word óf 'n inspuiting in u skouer kan hê om die senuwees na u arm te verdoof. U het die inspuiting gekies, en dus nooi ons u nou om aan hierdie studie deel te neem. U deelname behels slegs dat, voor ons u in u skouer inspuit, ons plakkers op u voorkop plak wat verbind is aan 'n masjien wat “slaperigheid” meet. Ons sal niks anders doen wat verskil van hoe ons gewoonlik hierdie inspuiting in die skouer toedien om die senuwees te verdoof nie, buiten om te monitor hoe wakker u voor die inspuiting is en dit met die “slaperigheid” na die inspuiting te vergelyk. Ons sal dit vir 'n uur voor die operasie self doen. Vandat u in die teater aankom totdat die operasie afgehandel is, sal óf ek óf my kollega by u bly om seker te maak dat u gemaklik en veilig is. Ons sal dit doen deur u te monitor soos ons enige pasiënt wat narkose ontvang sou monitor, deur u polsslag en bloeddruk te meet.

Is daar enige risiko's verbonde aan u deelname aan hierdie navorsingsprojek?

U instemming om aan die studie deel te neem, hou geen bykomende risiko's vir u in nie.

Daar is egter 'n paar risiko's verbonde aan die inspuiting in die skouer waarvan ons deeglik bewus is en wat ons altyd probeer vermy.

Die risiko's verbonde aan hierdie prosedure sluit die volgende in:

- Die risiko dat u te veel van die verdowingsmiddel kan ontvang. Die verdowingsmiddel word bupivacaïne genoem. Indien te veel toegedien word, of indien dit per abuis direk in 'n aar ingespuut word, kan dit die hart en/of die brein beïnvloed. Dit kan die hart snaaks laat klop en kan selfs die hart laat stop. Dit kan ook vreemde sensasies in u hele liggaam veroorsaak, selfs in u mond, en kan toevale/aanvalle tot gevolg hê. Ons vermy hierdie risiko deur die dosis wat ons vir u liggaamsgrootte nodig het akkuraat te bereken en deur baie versigtig te wees om nie die medisyne in die bloed in te spuit nie maar net rondom die senuwees. Indien u enige van die simptome ervaar, het ons die nodige medikasie om hierdie moontlike neue-effekte te behandel.
- Die risiko dat u long per abuis raakgesteek word wanneer die inspuiting toegedien word. Die risiko hiervan is baie klein, maar indien dit sou gebeur kan dit maklik behandel word.
- Die risiko dat die medikasie in die senuwee in plaas van daarom ingespuut word. Dit kan 'n vreemde gevoel, soos wanneer 'n mens se voet slaap, tot gevolg hê; dit gaan gewoonlik binne 6 weke weg. Omdat u wakker is terwyl ons die inspuiting toedien, kan u ons help deur te sê indien daar enige skerp pyn is, wat 'n goeie aanduiding is dat ons te na aan die senuwees is. Ons gebruik ultraklank wanneer ons die inspuiting toedien, wat baie help om seker te maak dat ons presies in die area om die senuwees inspuut.

Indien u enige van hierdie simptome ondervind of vir 'n buitengewoon lang tyd 'n doodse gevoel ervaar, kan u met dr. Rubendren Naidoo, die studiedokter, by die kontakbesonderhede hier bo in verbinding tree.

Hierdie risiko's word met die inspuiting in die skouer geassosieer. Die enigste ander ding wat ons in hierdie studie sal doen, is om u "slaperigheid" met die plakkers op u voorkop te meet. Weereens, u instemming om aan die studie deel te neem, hou geen bykomende risiko's vir u in nie.

Ons sal u te alle tye monitor en indien enige van die risiko's hier bo genoem plaasvind, sal ons die nodige doen om u te help.

In geval van enige komplikasie is daar riglyne en reëls wat gebruik word om die situasie te evalueer. Hierdie riglyne staan bekend as die riglyne vir Suid-Afrikaanse Goeie Kliniese Praktijk van 2006, 'n stel reëls rakende navorsing op pasiënte wat deur die Minister van Gesondheid

goedgekeur is en gereguleer word. Artikel 4.11 van hierdie riglyne handel spesifiek oor vergoeding in die geval van enige ernstige permanente besering. Die kans dat u 'n komplikasie sal hê, is skraal, maar indien dit sou gebeur en permanente besering tot gevolg sou hê, sal ons hierdie riglyne volg ten einde te verseker dat u toepaslik vergoed en veilig is. Hierdie riglyne, asook die Gesondheidsnavorsingsetiekkomitee, vereis dat indien u aan hierdie studie deelneem, u deur versekering gedek word, wat die Universiteit Stellenbosch wel het.

Wie sal toegang hê tot u mediese rekords?

Alle inligting wat versamel word, sal vertroulik hanteer word. In gevalle waar ons die studie in 'n vaktydskrif publiseer sodat ander daaruit kan leer, sal u besonderhede nie in die vaktydskrifartikel verskyn nie. U besonderhede sal anoniem bly. Slegs die studiedokters wat by hierdie projek betrokke is, sal toegang tot u inligting hê. U inligting sal veilig bewaar word ooreenkomstig die riglyne uiteengesit in artikel 6.5 van die riglyne vir Suid-Afrikaanse Goeie Kliniese Praktyk van 2006, 'n stel reëls rakende navorsing op pasiënte wat deur die Minister van Gesondheid goedgekeur is en gereguleer word.

By geleentheid sal die etiekkomitee wat die navorsing rig wat aan die Universiteit Stellenbosch gedoen word 'n inspeksie onderneem ten einde te verseker dat ons studie veilig is. Hulle kan dan ook toegang tot u inligting versoek. Die kontakbesonderhede van die etiekkomitee word hier onder verskaf indien u enige vrae het.

Sal u betaal word vir deelname aan die navorsingsprojek en is daar enige koste verbonde aan deelname?

U sal nie betaal word vir deelname aan die navorsingsprojek nie. Deelname aan die navorsingsprojek sal u niks kos nie.

Is daar enigiets anders wat u moet weet of doen?

U kan Dr Rubendren Naidoo kontak by tel 021 938 5142 indien u enige verdere vrae het of enige probleme ondervind.

U kan die Gesondheidsnavorsingsetiek-administrasie kontak by 021 938 9820 indien u enige bekommernis of klage het wat nie bevredigend deur u studiedokter hanteer is nie.

Verklaring deur deelnemer

Met die ondertekening van hierdie dokument onderneem ek,, om deel te neem aan 'n navorsingsprojek getiteld “ 'n Proefstudie om te bepaal of supraklavikulêre blokke van die bragiale plexus met 0.5% bupivakain die bewussynsvlak, soos gemeet deur middel van bispektrale indeksspektrofotometrie (BIS), verlaag

Ek verklaar dat:

- Ek hierdie inligting- en toestemmingsvorm gelees het of aan my laat voorlees het en dat dit in 'n taal geskryf is waarin ek vaardig en gemaklik mee is.
- Ek geleentheid gehad het om vrae te stel en dat al my vrae bevredigend beantwoord is.
- Ek verstaan dat deelname aan hierdie navorsingsprojek vrywillig is en dat daar geen druk op my geplaas is om deel te neem nie.
- Ek te eniger tyd aan die navorsingsprojek mag onttrek en dat ek nie op enige wyse daardeur benadeel sal word nie.
- Ek gevra mag word om van die navorsingsprojek te onttrek voordat dit afgehandel is indien die studiedokter of navorser van oordeel is dat dit in my beste belang is, of indien ek nie die ooreengekome navorsingsplan volg nie.

Geteken te (*plek*) op (*datum*) 2016.

.....

Handtekening van deelnemer

.....

Handtekening van getuie

Verklaring deur navorser

Ek (*naam*) verklaar dat:

- Ek die inligting in hierdie dokument verduidelik het aan
- Ek hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.
- Ek tevrede is dat hy/sy al die aspekte van die navorsingsprojek soos hierbo bespreek, voldoende verstaan.

- Ek 'n tolk gebruik het/nie 'n tolk gebruik het nie. (*Indien 'n tolk gebruik is, moet die tolk die onderstaande verklaring teken.*)

Geteken te (*plek*) op (*datum*) 2016.

.....

Handtekening van navorder

.....

Handtekening van getuie

Verklaring deur tolk

Ek (*naam*) verklaar dat:

- Ek die navorser (*naam*) bygestaan het om die inligting in hierdie dokument in Afrikaans/Xhosa aan (*naam van deelnemer*) te verduidelik.
- Ons hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.
- Ek 'n feitelik korrekte weergawe oorgedra het van wat aan my vertel is.
- Ek tevrede is dat die deelnemer die inhoud van hierdie dokument ten volle verstaan en dat al sy/haar vrae bevredigend beantwoord is.

Geteken te (*plek*) op (*datum*) 2016.

.....

Handtekening van tolk

.....

Handtekening van getuie

Appendix C- Informed consent translated into isiXhosa

INCWADANA ENGOLWAZI NGOMTHATHI-NXAXHEBA KUNYE NEFOMU
YEMVUMELWANO

ISIHLOKO SEPROJEKTHI YOPHANDO: Uphando lovavanyo lokumisela ukuba ingaba i-*supraclavicular brachial plexus* xa usebenzisa i-0.5% ye-*bupivacaine* ithomalalisa izinga lomqondo njengoko ikumlinganiselo we-*bispectral index* (efinyezwa njenge-BIS)

INOMBOLO YONXULUMANO: S15/01/008

UMPHANDI OYINTLOKO: Ugqir Rubendren Naidoo

IDILESI: Department of Anesthesiology and Critical Care, Stellenbosch University,
Tygerberg Academic Hospital, Fransie Van Zijl Avenue, Tygerberg, 7505

INOMBOLOYOQHAGAMSHELWANO: +27836555934 / +27219385142
placebo515@yahoo.com

Igama lesigulane :

Inombolo yeFolda :

Umhla wokuzalwa:

(ungafaka istikha sesigulane apha)

Ukwazisa kwiProjekthi yoPhando: Amalungelo noxanduva lwakho

Uyamenywa ukuba athathe inxaxheba kwiprojekthi yophando. Nceda thatha ixesha lokufunda ulwazi oluvezwe apha, oluza kuthi luchaze iinkcukacha zale projekthi. Nceda buza nayiphi na imibuzo emalunga nayiphi na indawo ongayiqondiyo ngokupheleleyo kubasebenzi besi sifundo okanye kugqirha. Kubaluleke kakhulu ukuba waneliseke ngokupheleleyo yinto yokuba ucacelwe kakuhle ukuba yintoni ebangwa sesi sifundo kwaye ungabandakanyeka njani. Kwakhona, ukuthatha kwakho inxaxheba kungentando yakho ngokupheleleyo kwaye ukhululekile ukuba ungarhoxa ekuthatheni inxaxheba. Ukuba uthi hayi, oku akusayi kuchaphazela ukungavumi kwakho nangayiphi na indlela. Ukwakhululekile ukuba uyeke kwesi sifundo nanini na, nkqu nokokuba ubuvumile ukuthatha inxaxheba ekuqaleni.

Olu phando luvunywe ziinqobo ezisesikweni zeKomiti yoPhando Lomntu kwiYunivesithi yaseStellenbosch kwaye luza kwenziwa ngokwemigaqo esesikweni yophando elamkelekileyo kwiSaziso seHlabathi sika-Helsinki, imiGaqo eLungileyo yoMzantsi Afrika yokuSebenza eKliniki kunye neBhunga lezoPhando ngamaYeza (MRC) imiGaqo yeNqobo yezoPhando.

Simalunga nantoni esi sifundo sophando?

Amaxesha amaninzi, endaweni yokuba ulaliswe ngokupheleleyo kwaye wenziwe uphefumle ngoomashini xa usenziwa utyando olulula engalweni, senza ndindisholo imithambo-luvo ebonelela ngemvakalelo engalweni ngelixesha uhleliyo ungalelanga. Sikwenza oku ngokukuhlaba inaliti eneyeza lokwenza ndindisholo elibizwa ngokuba “sisithomalalisi-ntlungu” malunga neeqela nemithambo-luvo esegxalabeni nethi yenze ingalo yakho ibendindisholo yonke. Sikwenza oku rhoqo kwaye esi sakhono sisakhono esamkelekileyo kakhulu. Umthambo-luvo osengalweni uza kukhubazeka okwexesha ungakwazi ukufumana imvakalelo okanye ukushukuma ngokufanelekileyo kangangeeyure ezi-6 ukuya kwezi-12.

Siqaphele ukuba olu hlobo lwesilalisi sivumela ukuba izigulane zigoduke kwakamsinyane emva kotyando kwaye ziba nolawulo olungcono lweentlungu ixesha elide emva kotyando. Oku kukwathetha ukuba incutshe yomlalisi (ugqirha ofaka inaliti enechiza lokulalisa) akanasizathu sokusebenzisa izixhobo zokuxhasa ukuphefumla nobomi ngexesha kusenziwa utyando olulula. Ngokuvingcela umthambo-luvo, kufuneke sisebenzise iziyobisi ezinjenge-*morphine* kancinane nethi ichaphazele ukusebenza kwemiphunga nentliziyo (ithoba ukuphefumla kunye noxinzelelo lwegazi).

Siqaphele ukuba kwezinye iindawo zomzimba, xa lamachiza okwendindisholo efakiwe, njengaxa abafazi bebeleka banikwa i-“epidurals” ukuze bajongane nokulunywa, la machiza okwenza ndindisholo aphelisa iintlungu de ngamanye amaxesha izigulane zizive zisozela.

Sifuna ukujonga ukuba ufakwe inaliti egxalabeni enamachiza okwenza ndindisholo ungeva zintlungu ingaba anefuthe elifanayo kusini na lokwenza ukuba uzive undongondongo bubuthongo.

Kutheni umenyiwe ukuba uthathe inxaxheba?

Ubhukishelwe utyando engalweni yakho. Ke ngoko udinga “isithomalalisi-ntlungu”. Incutshe yomlalisi ikucebise ukuba “ungalaliswa ngamachiza” okanye ungafakwa inaliti egxalabeni ukwenza ingalo yakho ibe ndindisholo. Uthe wakhetha ukuba ufakwe inaliti, kwaye ke ngoko uyamemwa ukuba ube yinxalenye yolu phando. Into oza kuthabatha ngayo inxaxheba kolu phando kukuba sikucele ukuba ngaphambi kokufakwa inaliti yesithomalalisi-ntlungu egxalabeni lakho, thina sibeka izitika apha ebunzi. Izitika ziza kunxibelelana nomashini owenza umlinganiselo “wokulala” kwakho. Akukho nto siza kuyitshintsha kwindlela esifaka ngayo inaliti enamachiza okulalisa egxalabeni lakho ukuze kwenziwe ndindisholo umthambo-luvo wengalo yakho ngaphandle nje kokubeka esweni ukuba uvuke kangakanani ngaphambi kwenaliti naxa kuthelekiswa nenqondo lokulala kwakho emva kwenaliti. Siza kwenza oku kwiyure ngaphambi kotyando lwenziwe.

Ukusukela ngexesha ungena kwigumbi loqhaqho de uya kugqiba utyando. Mna okanye ugxa wam uza kuhlala nawe ukuze siqinisekise ukuba uzolile kwaye ukhuselekile. Siza kwenza oku ngokuthi sibeke iliso kangangoko sisenza nakwesiphi na isigulane xa sifakwe isithomalalisi-ntlungu, ngokuthi siphonononge ukubeka komthambo kunye nocinizelelo lwegazi.

Ingaba zikho iingozi ezibandakanyekayo ekuthatheni kwakho inxaxheba kolu phando?

Akukho mngcipheko wongezelekileyo ngakuwe ngokuthabatha inxaxheba kolu phando. Nangona kunjalo, nangaliphi na ixesha ufakwa inaliti egxalabeni, kukho umngcipheko othile esiwaziyo thina kwaye sisoloko siwuphepha kangangoko.

Umngcipheko omalunga nolu tyando ubandakanya:

- Imingcipheko yokufumana amachiza amaninzi othomalaliso-zintlungu. Igama lesithomalalisi-ntlungu sibizwa ngokuba yi-*bupivacaine*. Ukuba ifakwe kakhulu okanye ithe yafakwa ngqo kwimithambo yegazi, ingachaphazela intloko kunye / okanye ubuchopho. Ingabangela ukuba intliziyo ibethe ngendlela engaqhelekanga okanye ivele ime ingabethi. Ingenza ukuba uzive ngendlela eyahlukileyo umzimba lo wakho wonke kuqukwa nomlomo, kwaye ingakhokelela kukuxhuzula. Sikuphepha oku ngokuthi sibale ngokuchanekileyo umyinge ongadingwa ngumzimba wakhe ngokobungakanani bawo kwaye siqinisekisa ukuba sifaka ngenaliti amachiza alingana nomzimba wakho kwindawo enemizwa singawafaki egazini. Ukuba uthe wabonakalisa naziphi na iimpawu, sinawo amanye amachiza akulungeleyo ukulungisa naziphi na iimpawu ezingafanelekanga ezingakho.
- Umngcipheko wokugqabhuza umphunga wakho ngeli lixa ufakwa inaliti. Lo mngcipheko unamathuba ambalwa gqitha ukuba ungenzeka kodwa ke ukuba uthe wenzeka, unganyangwa lula.
- Umngcipheko wokufaka amachiza ngenaliti kumthambo-luvo endaweni yokuwafaka kwindawo engqonge umthambo-luvo. Oku kungakhokelela kwimvakalelo engaqhelekanga yeepini neenaliti; nethi iphele emva kweeveki ezi-6. Ngokuthi sikwenze ube uvukile ngelixa sifaka inaliti, uya kusixelela ukuba kukho naziphi na iintlungu eziqubulisekileyo, nesisikhokelo sokuba sibe kude kangakanani umthambo-luvo. Sisebenzisa umashini we-*ultrasound* ukufaka amachiza ngenaliti, nonceda kakhulu ekubeni sazi ukuba sihlaba ngqo kwindawo engqonge umthambo-luvo.
- Ukuba uziva uneempawu kwaye kubandindisholo ixesha elide elingalindelekanga, nceda uqhagamshelane noGqirha Rubendren Naidoo, ugqirha wophando kwiinkcukacha zakhe zomnxeba ezibhalwe ngezantsi.
- Lo mngcipheko unxulunyaniswa nokufakwa inaliti egxalabeni. Into eyahlukileyo kuphela kolu phando kukuba siza kwenza umlinganiselo wokulala kuphela ngezitika kwibunzi lakho.

Kwakhona akukho mingcipheko yongezekileyo engangumphumela wokuvuma kwakho ukuthabatha inxaxheba kolu phando.

- Siza kubeka iliso kuwe ngalo lonke ixesha kwaye ukuba nawuphi na umngcipheko ochaziweyo apha ngentla uyenzeka, siza kwenza konke okuyimfuneko ukukunceda.
- Kwisiganeko sayo nayiphi na ingxaki enokwenzeka, kukho izikhokelo kunye nemigaqo emele ukusetyenziswa ukuphonononga imeko. Ezi zikhokelo zibizwa ngokuba zizikhokelo ze-South African Good Clinical Practice (SAGCP) zika-2006 neziyingqokelela yemigaqo malunga nophando kwizigulane, kwaye zaphunyezwa zamiselwa ngumPhathiswa weMpilo. Icandelo 4.1.1 wezi zikhokelo uthetha ngqo ngembuyekiso ukuba kubekho umonzakalo ongunomphelo omkhulu. Amathuba okuba nengxaki anqabile kakhulu kodwa ke ukuba oku kungenzeka kwaye kwenze umonzakalo osisigxina, siza kulandela ezi zikhokelo zidandalazisiweyo ukuqinisekisa ukuba sikunika imbuyekiso ngokufanelekileyo nangokukhuselekileyo. Ezi zikhokelo, ngokuhambisana nekomiti yophando kwezempilo, zithi ukuba uthabatha inxaxheba kuphando, ukhavarishiwe yi-inshorensi yeYunivesity yaseStellenbosch.

Ngubani uza kufumana ingxelo yakho yamayeza?

Lonke ulwazi oluya kuqokelelwa luya kugcinwa luyimfihlo. Kwimeko apho sipapasha uphando kwijenali sisenzela abanye ukuba bafunde, iinkcukacha zakho azisayi kufakwa kwiphepha lejenali. Iinkcukacha zakho ziza kuhlala zingaziwa mntu. Ngogqirha bophando kuphela abaya kufikelela kulwazi ngawe, noluya kube lugcinwe ngokukhuselekileyo ngokungqinelana nezikhokelo ezidandalaziswe kwicandelo 6.5 lezikhokelo zeSouth African Good Clinical Practice (SAGCP) zika-2006 neziyingqokelela yemigaqo malunga nophando kwizigulane, kwaye zaphunyezwa zamiselwa ngumPhathiswa weMpilo.

Ngamaxesha athile, ikomiti yeenqobo zophando ekhokela uphando olwenziwa kwiYunivesity yaseStellenbosch iye ihlole ukuqinisekisa ukuba uphando lwethu lukhuselekile kwaye bangacela ukufikelela kwiinkcukacha zakho. Iinkcukacha zoqhagamshelwano zekomiti yeenqobo zophando ziqhotyoshelwe apha ngezantsi ukuba ingathanda ukubuza nayiphi na imibuzo onayo.

Ingaba uza kuhlululwa ngokuthabatha inxaxheba kolu phando? Ingaba kukho iindleko oza kubanazo?

Awusayi kuhlululwa ngokuthabatha inxaxheba kuphando. Akukho zindleko zibandakanyekayo ngakuwe ngokuthabatha inxaxheba.

Ingaba ikho enye into ekumele uyazi okanye uyenze?

Ungaqhagamshelana noGqir Rubendren Naidoo kule nombolo yomnxeba 021 938 5142 ukuba unemibuzo engaphaya okanye uhlangabezana neengxaki.

Ungaqhagamshelana neKomiti yoPhando Lomntu kwa-021-938 9207 ukuba unenkxalabo okanye izikhalazo ezingasonjululwanga kakuhle ngugqirha wakho wophando .

Isifungo somthathi-nxaxheba

Ngokutyikitya ngezantsi, Mna ndiyavuma ukuthatha inxaxheba kuphando olubizwa ngokuba (Uphando lovavanyo lokumisela ukuba ingaba i-*supraclavicular brachial plexus blocks* xa usebenzisa i-0.5% ye-*bupivacaine* ithomalalisa izinga lomqondo njengoko ikumlinganiselo we-*bispectral index spectrophotometry* (efinyezwa njenge-BIS)).

Ndazisa ukuba:

- Ndilufundile okanye ndalufunda olu lwazi kunye nefomu yemvumelwano kwaye ibhalwe ngolwimi endiliciko nendikhululekileyo kulo
- Bendinalo ithuba lokuba ndibuze imibuzo kwaye yonke imibuzo yam iphendulwe ngokwanelisayo.
- Ndiyakuqonda ukuba ukuthatha inxaxheba kolu phando kube kukuzithandela kwam kwaye andikhange ndinyanzelwe ukuba ndithathe inxaxheba.
- Ndingakhetha ukulushiya uphando nanini na kwaye andisayi kohlwaywa okanye uqal' ugwetywe nangayiphi indlela.
- Usenokucelwa ukuba ulushiye uphando phambi kokuba luphele, ukuba ugqirha wophando okanye umphandi ukubona kuyinzuzo kuwe, okanye ukuba andisilandeli isicwangciso sophando, ekuvunyelenwe ngaso.

Kutyikitywe e-(indawo) ngo-(usuku) 2016.

.....

Umtyikityo womthathi-nxaxheba

.....

Umtyikityo wengqina

Isifungo somphandi

Mna (*igama*) ndiyafunga ukuba:

- Ndilucacisile ulwazi olu kweli xwebhu ku-.....
- Ndimkhuthazile ukuba abuze imibuzo kwaye athathe ixesha elifanelekileyo ukuba ayiphendule.
- Ndiyaneliseka kukuba uyakuqonda ngokwanelisayo konke okumalunga nophando okuxoxwe ngasentla.
- Ndisebenzise/andisebenzisanga toliki. (*Ukuba itoliki isetyenzisiwe kumele ityikitye isaziso ngezantsi.*)

Kutyikitywe e-(indawo) ngo-(usuku) 2016.

.....
Umtyikityo womphandi

.....
Umtyikityo wengqina

Isifungo setoliki

Mna (*igama*) ndazisa ukuba:

- Ndicende umphandi (*igama*) Ekucaciseni ulwazi olu lapha kweli xwebhu ku-(*igama lomthathi-nxaxheba*) ndisebenzisa ulwimi lwesiXhosa.
- Simkhuthazile ukuba abuze imibuzo kwaye athathe ixesha elifanelekileyo ukuba ayiphendule.
- Ndimxelele eyona nto iyiyo malunga nokunxulumene nam.
- Ndiyaneliseka kukuba umthathi nxaxheba ukuqonda ngokupheleleyo okuqulathwe lolu xwebhu lwemvumelwano eyazisiweyo kwaye nemibuzo yakhe yonke iphendulwe ngokwanelisayo.

Kutyikitywe e-(*indawo*) ngo-(*usuku*) 2016.

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Umtyikityo wetoliki

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Umtyikityo wengqina

Appendix D: Password code sheet

1	Attach patient details here
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Appendix F

Data Collection Sheet

Data set code:

Age	
Gender	
Weight	
ASA score	
Bupivacaine batch number/exp date	
Bupivacaine dose	
Defibrillator/intralipid checklist	
Chronic/traumatic illness	

Time	Time (hh:mm)	Best BIS Score	O ₂ sats	BP	Pulse
Pre-block					
0 min					
10 min					
20 min					
30 min					
40 min					
50 min					
60 min					

Appendix G

Checklist for Treatment of Local Anesthetic Systemic Toxicity ²⁹

AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

The Pharmacologic Treatment of Local Anesthetic Systemic Toxicity (LAST) is Different from Other Cardiac Arrest Scenarios

- ☐ ☐ Get Help
- ☐ ☐ Initial Focus
 - ☐ ☐ Airway management: ventilate with 100% oxygen
 - ☐ ☐ Seizures suppression: benzodiazepines are preferred; AVOID propofol in patients having signs of cardiovascular instability
 - ☐ ☐ Alert the nearest facility having cardiopulmonary bypass capability
- ☐ ☐ Management of Cardiac Arrhythmias
 - ☐ ☐ Basic and Advanced Cardiac Life Support (ACLS) will require adjustment of medications and perhaps prolonged effort
 - ☐ ☐ AVOID vasopressin, calcium channel blockers, beta blockers, or local anesthetic
 - ☐ ☐ REDUCE individual epinephrine doses to <1 mcg/kg
- ☐ ☐ Lipid Emulsion (20%) Therapy (values in parenthesis are for 70kg patient)
 - ☐ ☐ Bolus 1.5 mL/kg (lean body mass) intravenously over 1 minute (~100mL)
 - ☐ ☐ Continuous infusion 0.25 mL/kg/min (~18 mL/min; adjust by roller clamp)
 - ☐ ☐ Repeat bolus once or twice for persistent cardiovascular collapse
 - ☐ ☐ Double the infusion rate to 0.5 mL/kg/min if blood pressure remains low
 - ☐ ☐ Continue infusion for at least 10 minutes after attaining circulatory stability
 - ☐ ☐ Recommended upper limit: Approximately 10 mL/kg lipid emulsion over the first 30 minutes
- ☐ ☐ Post LAST events at www.lipidrescue.org and report use of lipid to www.lipidregistry.org